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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,501	02/25/2004	Susan L. Acton	MPI98-052P1RDV10DV1M	3988

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MILLENNIUM PHARMACEUTICALS, INC.
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EXAMINER	
HUMPHREY, DAVID HAROLD	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,501	ACTON, SUSAN L.	
	Examiner	Art Unit	
	David Humphrey	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-64* is/are pending in the application.

4a) Of the above claim(s) *61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-60,63 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group III(a), claims 49-60 and 63-64, without traverse in the reply filed on 04/10/2006 is acknowledged.

2. Claims 49-64 are pending.

Claims 61 and 62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 49-60, 63, and 64 are examined on the merits.

Specification

3. Applicant is required to update the status (pending, allowed, etc.) of all parent priority applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate.

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 33, lines 19 and 34, for example.

Sequence Listing

5. The Examiner notes that the paper copy of the sequence listing can be found with the specification as pages 80-111. The Examiner also notes that CRF of the sequence listing has also been supplied by Applicants. However, Applicants still need to provide a statement that the paper copy and the CRF are identical and that no new matter has been introduced. SEE 37 C.F.R. § 1.821 paragraphs (f) and (g).

Title of the Invention

6. The title of the invention is not descriptive.. A new title is required that is clearly indicative of the invention to which the claims are directed. See MPEP § 606.01. In addition, Applicant should avoid the use of the word "novel" in the title, as patents are presumed to be novel and unobvious.

Claim Rejections - 35 USC § 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 49-60, 63, and 64, are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus. " (See MPEP 2164).

In the instant case, the claims are drawn to an isolated antibody that specifically binds to a polypeptide selected from the group including: (c) a polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence contained in the plasmid deposited with ATCC as Accession number 203309. There are no functional requirements for the polypeptide encoded by a nucleotide sequence that is at least 95% identical to the sequence contained in the plasmid deposited with ATCC as Accession number 203309. Since the polypeptides encoded by a sequence which is at least 95% identical to ATCC 203309 can have any function or even no function, the claims encompass a large genus of antibodies to those polypeptides. The specification does not indicate which regions need to be conserved within the plasmid sequence and which positions can tolerate

mutations or differences. Therefore, Applicant is not in possession of a genus of antibodies that bind to a polypeptide encoded by the nucleic acid molecule comprising a sequence that at least 95% identical to ATCC Accession number 203309.

Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, 1st Written Description Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column). In the instant case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing

identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

9. Claims 49-60, 63, and 64, are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line which contains the plasmid ATCC Accession number 203309 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell

line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line.

The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR §§1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability o the biological material at the time of deposit will be made (see 37 CR §1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to MPEP §2400 in general, and specifically to §2144.05.

10. Claims 49-51, 53-57, 59, 60, 63, and 64, are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for an isolated antibody that binds to amino acid residues 5-164 of SEQ ID NO: 8, an isolated antibody, or fragment thereof, that specifically binds to (a) any polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 8, (b) any polypeptide encoded by the nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO: 7 or 9, does not reasonably provide enablement for an isolated antibody, or fragment thereof, that specifically binds to (c) any polypeptide encoded by a nucleic acid molecule comprising the nucleotide sequence contained in the plasmid deposited with ATCC as Accession Number 203309. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening.

However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not 'experimentation'. " (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims and the nature of the invention: Claims 49-51, 53-57, 59, 60, 63, and 64, require the antibody to bind to (c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleic acid comprising the nucleotide sequence contained in the plasmid ATCC Accession number 203309. The claims encompass antibodies that bind to any polypeptide encoded by a nucleic acid at least 95% identical to ATCC Accession number 203309.

The amount of direction provided by the inventor and the existence of working examples: There is insufficient guidance and direction as to how to make and use antibodies, wherein the antibodies bind any polypeptide comprising an amino acid sequence that is at least 95% identical to any polypeptide encoded by a nucleic acid which is at least 95% identical to a nucleic acid deposited with ATCC as Accession number 203309.

The specification does not provide sufficient guidance as to which of the nucleic acids may be changed. In addition, the encoded polypeptide is not required to retain any functional activity. In addition, the term "comprising" in claims 49 and 55 is open-ended and expands the amino acid sequence encoded by ATCC 203309 to include additional non-disclosed amino acids.

The state of the prior art and the level of predictability in the art: The relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) is not well understood and is not predictable. Rost et al. (Current Opinion in Biotechnology 7: 457-461, 1996) teach that in general protein three-dimensional structure cannot be predicted from sequence, see page 457, left column, "What can theory predict of protein structure?", lines 1-2.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support Applicant's claim to a genus of antibodies that bind to polypeptides comprising polypeptides that are encoded by nucleic acids that are at least 95% identical to those encoded by ATCC Accession number 203309.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure: Due to the breadth of the claims, the lack of guidance, and the unpredictability in the art, one of ordinary skill would be required undue experimentation to determine which modifications would be

acceptable to retain occluding structural and functional activity. In addition, since the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require an undue amount of experimentation for one of skill in the art to determine which antibodies bind to polypeptides encoded by nucleic acids that are at least 95% identical to those of ATCC Accession number 203309. Therefore, the scope of the claimed antibodies is not commensurate with the enablement provided by the disclosure with regard to the number of possible amino acid sequences encompassed by the claimed invention. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a peptide's amino acid sequence, and, in turn, nucleic acid sequence and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the peptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the peptide's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the

specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David Humphrey, Ph.D.

June 2, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER